

Amendments to the Specification:

Please replace the abstract with the enclosed ABSTRACT.

Please replace the first and second paragraphs under the BRIEF DESCRIPTION OF THE DRAWINGS on page 21 with the following two amended paragraphs:

~~Fig. 1 is~~ Figs. 1A – 1B show a schematic illustration of an assay device in a manner of performing the assay in accordance with an embodiment of the invention;

~~Fig. 2 is~~ Figs. 2A – 2D show a schematic illustration of an assay device in a manner for performing the method in accordance with an embodiment of the invention;

Please replace the paragraph bridging pages 26 and 27 with the following amended paragraph:

In all the embodiments shown in Figs. 3A-3E, a recognition moiety is immobilized on at least one electrode of an assay set. Against the case of the embodiments of the assay sets 222 and 234 and 244 shown in Figs. 4A-4C, no recognition moiety is immobilized on the respective electrodes 224 and 226, 236 and 238 and 245 and 246. Rather, in this case, each of the assay sets 222, 234 and 244 have a substrate member 228, 240 and 247, respectively, which are other than the electrodes, on which the respective recognition moieties 230, 242' and 242" and 248 are bound. In the case of assay set 222, immobilized on member 228 is a single recognition moiety 230, which in this specific embodiment is an antibody directed to an epitope of target 232 (the target may be a nucleic acid sequence, a polymer, a

polypeptide, etc.). In the case of assay set 234, member 240 has immobilized thereon two oligonucleotide substrates 242' and 242" which are complementary to portions of target nucleic acid sequence 243. In both cases, after binding to the recognition moieties, a conductive bridge between the two electrodes of the assay sets is formed by a non-specific or semi-specific binding or association and typically by growth of a conductive layer from nucleation centers present on the targets or on complexes between targets and recognition moieties. In the case of assay set 244, after the oligonucleotide target 249 binds to the recognition moiety 248, it serves a template for synthesis of other nucleic acid sequences, and this synthesis eventually forms a path 249A between the two electrodes 245 and 246.

Please replace the paragraph bridging pages 27 and 28 with the following amended paragraph:

Fig. 6 shows the manner of determining concentration of a target in a sample in accordance with an embodiment of the invention. Each of electrodes 258 and 259 of assay set 250, has immobilized thereon a plurality of recognition moieties 260 and 261, respectively. After contact with a target 264, one or more paths between the electrodes form. In a case of low concentration of the target 264 (b1), a small number of paths forms in a given time period (illustrated here by a single path 266) and in the case of a high concentration (b2), a large number of paths, illustrated here by six paths 268 formed within the same time period. After steps for processing the paths to yield conductive bridges are carried out, it is clear that the measured resistance during the same time period is lower in the case of a high concentration as compared to a low concentration. This difference in the

potential/current relationship can thus serve as a measure (after proper calibration) of concentration of the target 264 in a sample.

Please replace the third paragraph on page 32 with the following amended paragraph:

Reference is now being made to Fig. 12, illustrating a device and method of the invention wherein the conductive bridge is formed by depositing a conductive polymer PPV, (poly-p-phenylene vinylene). Electrodes 400, may be the same as electrodes 300 shown in Fig. 10. The first two steps of the detection method (steps (a) and (b)) may be identical to the corresponding steps in Fig. 10 (identical components have been given a reference numeral with the same last two digits as the corresponding components in Fig. 10: e. g. 402 is the same as 302, 404 as 304, etc.). The formed path 412 may be strengthened, similarly as above, by covalent binding of DNA 410 to the recognition moieties 406 and 408 to yield a path 414 connecting the two electrodes (step (c)).

Please replace the first four paragraphs under the Example 12 heading on page 46 with the following four amended paragraphs:

In Fig. 21 (A) two conducting electrodes 502a are defined on an insulating substrate 501. In Fig. 21 (B) a monolayer of short, single-stranded oligonucleotides 503 is constructed in the gap between a pair of electrodes 502 of the assay device. The sequence of the oligonucleotides is complementary to the sequence of the target

to be deleted. The oligonucleotides have a dideoxy base at their 3'terminus and are therefore incapable of being extended with nucleic bases by use of transferase.

Fig. 21 (C) shows that upon contacting said assay device with the sample, the target oligonucleotide 504a binds to the recognition moiety 503 thus forming a recognition group (double-stranded DNA) 505. Different post-hybridization treatments such as washing at different temperatures and different salt concentrations ensure high selectivity in duplex formation.

In step (D), the assay device bearing the DNA duplex is contacted with a solution containing transferase and biotinylated bases which induces the elongation of the DNA skeleton at the 3'-deoxy site 506a.

In a subsequent step (step E), the assay device is exposed to a solution containing gold colloids coupled to streptavidin units 507. The resulting assay device bears DNA molecules with pendant gold colloids 508a.

Please replace the first paragraph under the Example 30 heading on page 62 with the following amended paragraph:

In some applications the ability of working with small sample volumes is of great advantage. For such purposes, embodiments making use of microfluidics techniques may be used. Fig. 37 is a cross-section through a chip which is similar (although not identical) to chip 1000 shown in Fig. 35 or 36. Identical elements to those shown in Fig. 25 have the same number. The base 1001, is composed of a doped-p-type silicon. Using a photoresist mask defined by photolithography, n-type parallel channels 1002 are defined using ion implantation techniques. The photoresist is then removed and the implanted area is thermally activated. A thin

silicon dioxide layer is then grown on the surface. A second photoresist mask is defined with holes for p-type implantation where the diode's anodes are to be created. The wafer is then p-type implanted to form p-type areas 1003, the photoresist is removed, and the implantation is thermally activated. A p-type area, relative to the n-type strips form the non-linear element 1004, needed for a multiplexed reading scheme. The silicon dioxide is then etched off and a new layer is grown 1005. Holes are opened in the silicon dioxide layer and bottom conductive electrodes 1006, low temperature oxide 1008, and upper aluminum electrodes 1007, are deposited by evaporation. Lift-off terminates this step. A third photoresist mask is defined with holes where the holes in the device are to be created. The detection site 1009 on chip 1000 is defined by a pair of electrodes 1006 and 1007 separated by a gap 1008. Gap 1008 will next be used as a hybridization site. Chip 1000 is placed between two solution ducts that serve as a reservoir 1010a for the sample solution. Solutions are driven back and forth between the two parts of the reservoir through the holes in the chip, thus ensuring efficient contact of sample with hybridization sites 1009 while maintaining low sample volume.